

5. The appropriate comparison cigarette depends on the type and objective of the study. For studies of smoke chemistry and toxicology, the key purpose of the comparison cigarette is to provide a benchmark. In this regard, the University of Kentucky reference cigarette 1R4F (1) is suitable. The construction of this cigarette is representative of products in the U.S. marketplace. Additionally, Steel et. al. (2) found that the mutagenic activity of the 1R4F cigarette is in the middle of the activities brands in the U.S. marketplace consistent with its tar delivery. The chemistry data derived in the Massachusetts benchmark study also shows that the 1R4F cigarette behaves similarly to brands representing the full range of cigarette construction parameters in the U.S. marketplace (3). Since the mutagenic activity and smoke chemistry yields fall in the middle of the U.S. marketplace and are equivalent on a tar delivery basis, the use of the 1R4F cigarette as a comparison provides information relevant to the market as well as a benchmark for comparison among studies. We are currently extending the work on the comparison of the University of Kentucky reference cigarettes in comparison to commercial brands. These tests will include both the 1R4F and 1R5F reference cigarettes and commercial products under different smoke collection conditions. In addition to smoke chemistry, the smoke will be tested in the Ames test and mammalian cell cytotoxicity tests. The results of these experiments will help guide our future use of the 1R4F reference cigarette.

For human studies of either exposure or health effects, the commercially available cigarettes would be preferred to the University of Kentucky reference cigarettes. These reference cigarettes are not flavored and have very different subjective characteristics than commercial products and would therefore not be suitable for the extended smoking period that would be required in such studies. Furthermore, for such studies, the person's own brand would be the best control as brand switching may result in a change in smoking behavior which could confound the results of the study depending on the study design.

[In response to the specific questions posed in question group 5, it is important to consider if the point of reference for harm reduction is on an individual basis or a population basis. Given that reduced-risk products are likely to have very different characteristics than the typical conventional cigarette products on the market today, it may be that the reduced-risk product would be substantially lower in some defined activity than any of the current conventional cigarette products, however.]

"A Kentucky reference cigarette?"

As noted above, based on current information, the University of Kentucky 1R4F reference is useful in studies of smoke chemistry and toxicology.

"The leading product based on market share?"

This approach would be of low utility except, perhaps, in some special cases. An issue with this approach is that the composition of this brand will change with time. This change could be a change within a particular brand or a change in the brand itself. For smoke chemistry and toxicology testing, it is important to have a consistent point of reference and for human studies the best reference is most likely the subject's current product. It may be, however, that for public communication the leading product may provide a useful frame of reference. For that purpose it would be necessary to know or adequately estimate the relative risk of that product.

"The lowest-risk product currently available?"

This approach also presents the difficulty of changes over time. It would also be important to define the particular risk; it may be that the characteristics of one product make it lower risk for cardiovascular effects but not change others and another product might address cancer but not others. There could, therefore, be a spectrum of lowest-risk product. — *matrix*

"Each individual smoker's brand at time of switching to the new product?"

As noted above, this is probably the best choice in human exposure and health effect studies.

"Each individual smokers dominant brand of his/her smoking history?"

Again, due to changes in brand composition and other characteristics over time, this would make for a poor reference point. For example, the delivery of X has gone from Y mg. of tar in 1970 to 2 mg. of tar in 1998.